Case report

Testicular choriocarcinoma: an unusual case of paraneoplastic thyrotoxicosis

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Introduction

The incidence of clinical hyperthyroidism has been reported as 0.8/1000 women per year, and it is less common in men. Causes of thyrotoxicosis include Grave’s disease, toxic multi-nodular goitre, toxic adenoma and thyroiditis. Rarely, thyrotoxicosis can arise as a paraneoplastic syndrome. In this setting, systemic symptoms of underlying malignancy may be wrongly attributed to primary hyperthyroidism leading to a delay in diagnosis. We report a rare case of thyrotoxicosis due to metastatic testicular choriocarcinoma that highlights the importance of a systematic clinical and biochemical assessment.

Case report

An 18-year-old male catering student initially presented to his family practitioner with back pain and dysuria and was diagnosed with a urinary tract infection. He was empirically prescribed two consecutive courses of antibiotics. He then developed a cough and dyspnoea attributed to community acquired lower respiratory tract infection, which was treated. His condition continued to deteriorate with a weight loss of 13.6 kg over a 6-week period. During this time, he had developed a large right testicular swelling, which was concealed. Routine thyroid function tests revealed a raised serum free thyroxine level and reduced thyroid-stimulating hormone (TSH) concentrations [free thyroxine 38.6 pmol/l (normal range (NR) 9.4–18.6), TSH <0.01 mU/l (NR 0.3–4.4)]. A few days later, he presented to our Emergency Department with haemoptysis. His past medical history was non-contributory and he had been prescribed no regular medications. He had stopped smoking 3 weeks prior to presentation.

On clinical examination, he appeared cachectic, diaphoretic and was tachycardic (120 bpm, sinus rhythm). There were no signs of goitre or dysthyroid eye disease. Occasional scattered crepitations were audible on chest examination. A large firm non-fluctuant right-sided scrotal swelling was present and the left testicle was not enlarged. Abdominal examination was otherwise normal.

Hypoxaemia was present with saturations of 91% on room air [pO2 10.60 kPa (NR 10.67–13.33)] on 5 L oxygen. His full blood picture, serum electrolytes, renal function and liver enzymes were normal. Serum corrected calcium was 2.14 mmol/l (NR 2.2–2.6). A chest X-ray revealed multiple bilateral ‘coin’ opacities. Serum β-human chorionic gonadotrophin (HCG) was measured and was found to be massively raised at 11 180 530.0 mIU/ml (NR 0–5). Computed tomography (CT) scan of chest demonstrated multiple large pulmonary metastases throughout both lung fields with hilar lymphadenopathy (Figure 1). Testicular ultrasound revealed a 10-cm solid right-sided scrotal mass, which appeared to entirely replace the right testicle, with localized invasion of
the spermatic cord. The left testicle was unremarkable. A clinical diagnosis of metastatic germ cell tumour of testis was made based on the findings of a solid testicular mass, multiple lung metastases and very high levels of serum β-HCG. His thyrotoxicosis was attributed to be a paraneoplastic phenomenon. He was treated with propanolol for symptomatic relief of hyperthyroidism. He was assessed by a consultant urologist and referred urgently to an oncologist with a specialist interest in gonadal tumours. He was classified as having a poor prognosis in view of his high level of β-HCG as a level >50,000 is regarded as a poor prognostic factor in the International Classification system. Transfer to the regional cancer centre for neo-adjuvant chemotherapy with a view to subsequent surgery was agreed. He was treated with intravenous fluids and allopurinol to reduce the impact of tumour lysis syndrome during chemotherapy. Thromboprophylaxis was contraindicated due to a high risk of spontaneous intrapulmonary haemorrhage. On the following day, he started emergency chemotherapy receiving carboplatin intravenously on Day 1 and etoposide intravenously over 3 days. His condition deteriorated and he developed respiratory failure within 24 h of starting chemotherapy. He was transferred to the Intensive Care Unit and required intubation and ventilation. CT pulmonary angiogram excluded pulmonary embolism and CT scan of brain showed no evidence of brain haemorrhage or metastases. His condition deteriorated steadily despite intensive support and he died 2 days later of respiratory failure.

**Discussion**

Seminomas account for ~50% of all testicular germ cell cancers. The remainder comprise teratomas or non-seminomatous germ cell tumours (NSGCT), with mixed tumours occurring in 10% of cases. The very high levels of β-HCG in this patient was strongly suggestive of choriocarcinoma histology, which is associated with a very poor prognosis and propensity for haematogenous metastases.
Paraneoplastic hyperthyroidism is a rare but recognized phenomenon associated with testicular germ cell tumours, although the exact prevalence is unknown. Germ cell tumours produce Human Chorionic Gonadotrophin (HCG), which is composed of α and β subunits. The α unit is similar to that of TSH, while the β unit is similar to luteinizing hormone. Thus, the massive rise in HCG associated with germ cell tumours can stimulate the TSH receptor as its very high concentration overcomes its lower affinity for the TSH receptor and induces thyrotoxicosis. In a small series, 7 of 17 patients with NGSCT having HCG levels >50 000 mIU/ml were found to have elevated serum thyroxine levels. In a recent study of NSGCT, 50% of patients with high HCG levels were found to have elevated thyroxine levels. In this small series, raised free thyroxine returned to within normal ranges within 26 days of starting chemotherapy in all patients.

Antithyroid therapy would, therefore, be of questionable value in similar cases of paraneoplastic thyrotoxicosis due to testicular tumours. Reported rates of carbimazole-induced agranulocytosis and neutropenia in primary hyperthyroidism have been quoted as 29.1 reports per million prescriptions. Even at this low rate, it is clear that antithyroid drugs could do more harm than good in such cases. At present, in any case, no evidence exists regarding the use of carbimazole in conjunction with chemotherapy in cases such as described here.

In conclusion, this case illustrates the rare occurrence of thyrotoxicosis arising as a paraneoplastic syndrome due to testicular choriocarcinoma. The presentation was significant in that the presenting clinical features were attributed to hyperthyroidism, but were likely to have been caused by his metastatic tumour. This case highlights the importance of a comprehensive clinical history and examination for all patients presenting with hyperthyroidism, especially in males. Poor risk choriocarcinoma is one of the most rapidly progressive malignancies, requiring emergency chemotherapy on diagnosis, and any delay in diagnosis and treatment can have grave consequences.

Conflict of interest: None declared.

References